Update
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OVINE PROGRESSIVE PNEUMONIA

Introduction

Ovine progressive pneumonia (OPP) is a slowly progressing viral disease of sheep that may affect any of several organ systems of the body. The disease usually occurs in sheep that are two to four years of age and may last for several months to a year with steady progression until death occurs. The clinical picture can vary from loss of weight ("thin ewe syndrome") to pneumonia with labored breathing, congested udder ("hardbag") with reduced or no milk production, arthritis with severe lameness, or encephalitis with paralysis of the rear quarters.

As the disease does not result in immediate death, affected sheep are often culled, causing great difficulty in assessing losses. In some flocks the loss may be slight; in others, depending upon the type of management, breed of sheep, strain of virus and climatic conditions, there may be extensive financial loss from lowered production and death. A preventive program, as discussed later in this paper, is currently the most feasible way of lowering the cost of OPP to the industry.

History

The respiratory form of OPP virus infection in sheep was first described in the United States in 1923 by Marsh in Montana and called progressive pneumonia. Since then, various modifiers such as Marsh's, Montana, chronic, and ovine have been used in the name. A report from South Africa in 1915 described a similar condition called "Graaff-Rinet" disease, after the region where it was found. This condition and the disease in the United States were compared and considered identical. A similar infection was described in France in 1940 and called "la bouhite," a local name for pulmonary lymphoma, and in Holland in 1943 as "zwoegerziekte," meaning lagging sickness. In Iceland, a pulmonary form of the disease was identified in 1947 as "maedi," meaning dyspnea or difficult breathing, and a paralytic form of the disease was identified in 1957 as "visna," meaning wasting. At first the different Icelandic forms were believed to be separate diseases, but later they were shown to be caused by the same virus. This resulted in the name maedi-visna that is used for the disease in many countries.

Characteristics Of The Agent And The Infection

Ovine progressive pneumonia is caused by a lentivirus (lenti = slow), which is a member of a group of viruses called retroviruses (retro = reverse) (Figure 1). These viruses are grouped together because they all contain reverse transcriptase, an enzyme necessary for their replication, and share similarities in their genetic makeup and structure. The retrovirus family of viruses causes slow progressive diseases, such as cancer in humans, cattle and cats; anemia in horses; arthritis in goats (CAE); and immunodeficiency syndromes in humans (AIDS) and cattle as well as OPP. With a few exceptions, these viruses are species specific, that is, known to infect only one or two closely related species. Experimentally, OPP and CAE viruses will each infect sheep and goats.

Lentiviruses have evolved into some very complex relationships with their hosts. Many viruses and bacteria affect only one body system and cause rapid disease with death or recovery of the host. In contrast, lentiviruses can induce disease in many body systems and establish lifelong

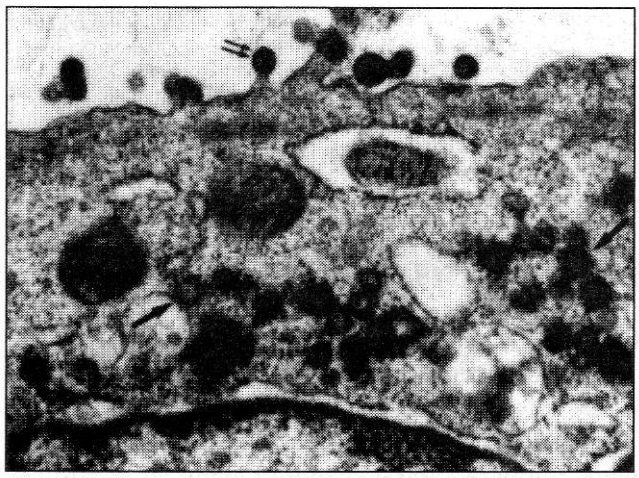

Figure 1. *Electron micrograph of a cell in culture that is infected with the OPP virus. Immature viral particles are present in the cytoplasm of the cell (arrows) and budding from the cell membrane (double arrows). The nucleus of the cell is at the bottom.*

infections that may or may not cause death. They do this by infecting and interfering with the immune functions of specialized cells, called macrophages and lymphocytes, and by changing their surface proteins to escape neutralizing antibodies. Both viral strategies prevent the host from clearing the virus from the body. They also make the development of vaccines against lentiviruses a very difficult challenge for scientists.

Although studies have shown conflicting results, some breeds of sheep probably are more susceptible than others to the effects of OPP virus and some strains of virus probably cause more disease problems than others. Sheep of the Texel, Border Leicester and Finnish Landrace breeds appear to develop more frequent and more severe OPP virus-induced disease than do other breeds, such as the Columbia, Rambouillet and Suffolk. All breeds of sheep produce antibodies against the virus, but the antibodies are not protective.

Prevalance

Except for Australia and New Zealand, the virus and disease are present in all major sheep producing countries of the world. Infection is common in all ages, breeds and sexes of sheep throughout North America. The proportion of sheep with serum antibodies to the virus ranges from 1 to 70 percent in different regions of the United States. Antibodies are found most frequently in sheep of the western (30 to 67 percent) and midwestern states (30 percent) with the lowest occurrence in the southern states (Texas 1 percent). A recent study found a 49 percent positive rate in the Rocky Mountain Region, whereas the northeastern region had the lowest rate, 9 percent.

Within a geographic region, positive sheep are not uniformly distributed but are concentrated in some flocks. One Idaho flock, composed of several breeds (Rambouillet, Targhee, Columbia, Polypay and Suffolk) has constantly had an infection rate of 47 percent for over a decade (1978-1988). Prevalence has been shown to increase in a flock with age of the sheep and length of exposure. There are no sex differences in infection rate.

Clinical Signs And Lesions

Sheep that are infected with the virus can exhibit a wide range of clinical signs. During early stages of infection no signs of disease are apparent. As time passes (two or more years) multiple signs and lesions may become apparent and can be attributed to involvement of one or more organ systems. In individual sheep, signs and lesions may occur alone or in any combination and are often accentuated around lambing time or during other times of stress. However, most infected sheep don't exhibit clinical disease.

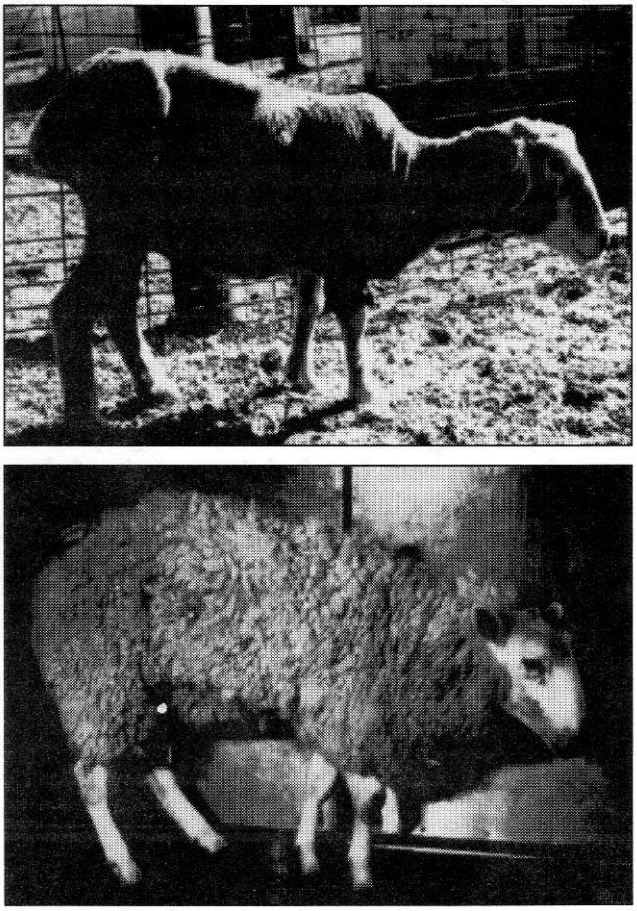

Figure 2a and 2b. *Sheep with OPP. Note severe wasting (2a) and swollen carpal (knee) joints (2b).*

A major sign, often the first, is a general loss of body condition often referred to as "thin ewe syndrome" (Figure 2a). The weight loss is progressive and occurs despite a normal appetite. The exact cause of this illthrift is not understood.

Clinical signs attributable to involvement of the respiratory tract are commonly associated with the disease. The rate of breathing at rest is increased and when moved the affected sheep ("lungers") tire easily and trail their flockmates. In the final phases of the disease, affected sheep will lie down much of the time. Coughing occurs when there is secondary pneumonia but nasal discharge is not often observed.

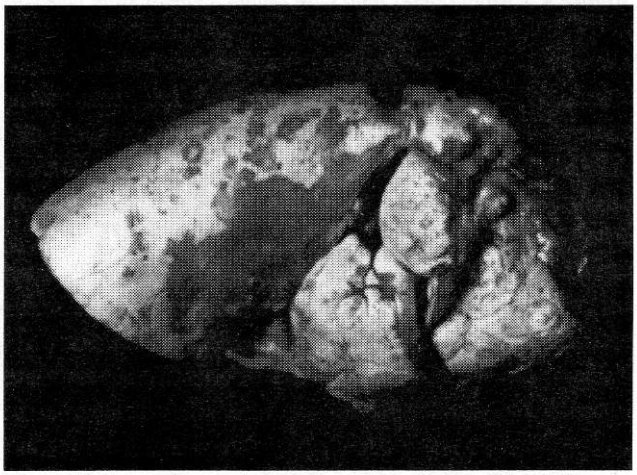

Figure 3. *Large, firm pale grey lungs from a ewe with OPP pneumonia. The small dark spots and large dark areas are caused by secondary bacterial infection.*

Respiratory tract signs are caused by changes within the tissues of the lungs. The membrane between air and blood, through which oxygen and carbon dioxide pass, becomes thickened with accumulations of lymphocytes and macrophages, scar tissue, and smooth muscle. These changes progressively inhibit exchange of gases. At death the lungs are two to three times normal weight, have a non-elastic, rubbery consistency and are a dull grayish blue to grayish brown color (Figure 3). Nodules, up to one-eighth inch in diameter, can be seen on the surface of the lungs and felt within the lung tissue. These nodules are located around the smaller airways and blood vessels of the lungs and consist of accumulations of lymphocytes (Figures 4 and 5). Lymph nodes in the chest can be up to 10 times their normal size.

The OPP virus also can affect the udder of the ewe causing it to enlarge and become firm ("hardbag"). Milk flow is reduced because of swelling and the accumulation of lymphocytes and

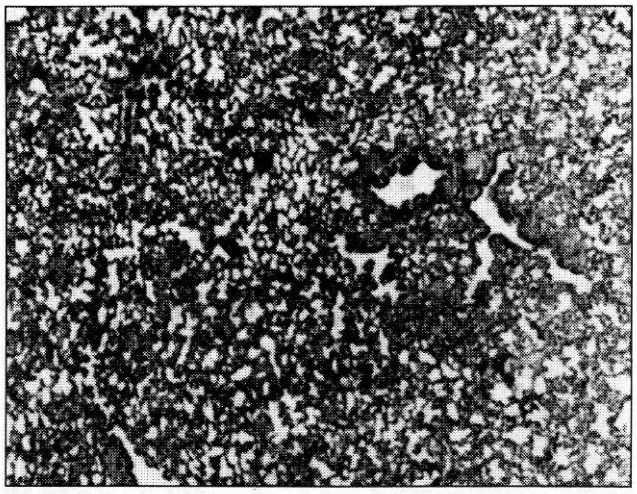

Figure 4. *Light micrograph of normal sheep lung. Compare the thin walls separating air spaces with those of infected sheep in Figure 5.*

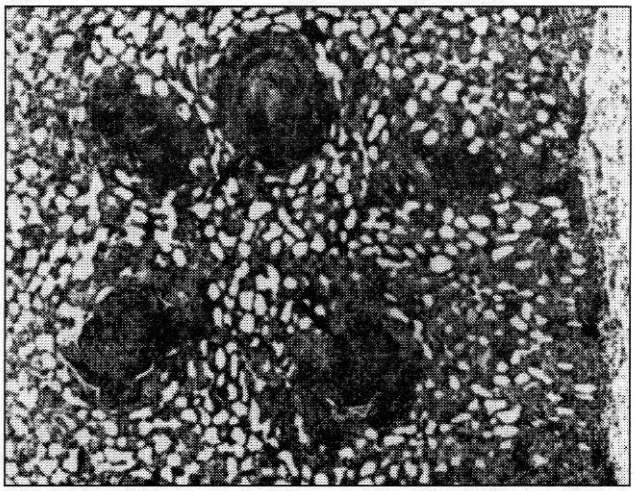

Figure 5. *Light micrograph of lung from sheep with OPP pneumonia. Large nodules of dark cells (lymphocytes and macrophages) surround air passages and blood vessels (arrows). Walls separating air spaces are thicker than normal.*

macrophages in the tissues surrounding the milk ducts (Figures 6 and 7). Some affected ewes do not produce enough milk, especially early in lactation, to nourish a lamb. The udder is not hot and painful nor are there abnormal milk secretions as seen with bacterial mastitis. All hardbag or firm udder is not caused by OPP virus infection: other causes are plant estrogens, hormonal imbalance and bacterial infections. With the latter causes, the firmness is usually reversible, with milk secretion increasing a few days after lambing or treatment. Hardbag caused by OPP virus is generally irreversible, although milk production usually increases slightly a few days after lambing, probably because of reduced swelling.

Arthritis may be associated with OPP virus causing lameness and swelling in one or more joints

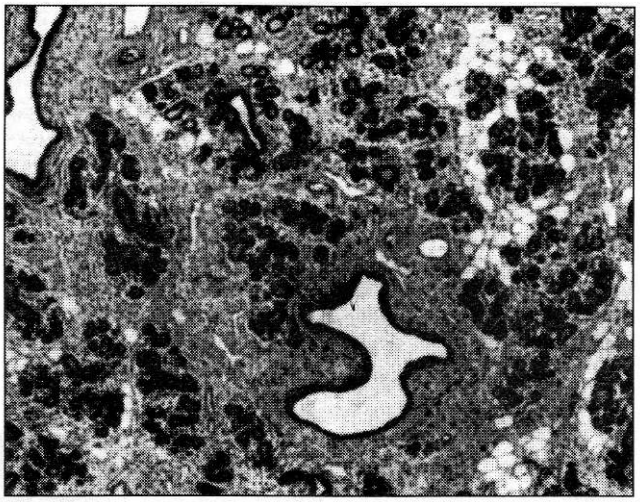

Figure 6. *Light micrograph of normal mammary tissue from a sheep.*

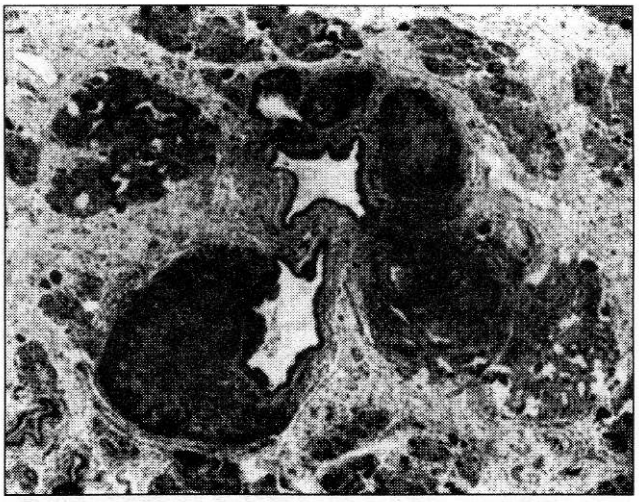

Figure 7. *Light micrograph of mammary tissue from a sheep with OPP mastitis. Large nodules of lymphoid tissue surround and compress the milk ducts.*

(Figures 2b and 8). "Knee" joints of the forelimbs and hock joints of the rear limbs are most commonly affected. This arthritis causes the joint capsule to thicken and become mineralized and the joint cartilage and bone to deteriorate. The longer the arthritis is present, the more marked is the damage to the cartilage and bone of the joint. Microscopically, lymphocytes and macrophages, as observed in the lung and mammary tissue, are present in the tissue of the joint (Figures 9 and 10).

Inflammation of the central nervous system (brain and spinal cord) is the least frequent form of OPP seen in the United States. When seen, the early signs are muscle quivering and loss of balance of the rear quarters. This slowly progresses to paralysis of the hind limbs with the sheep unable to stand. The brain and spinal cord appear normal when observed with the unaided eye, but microscopic

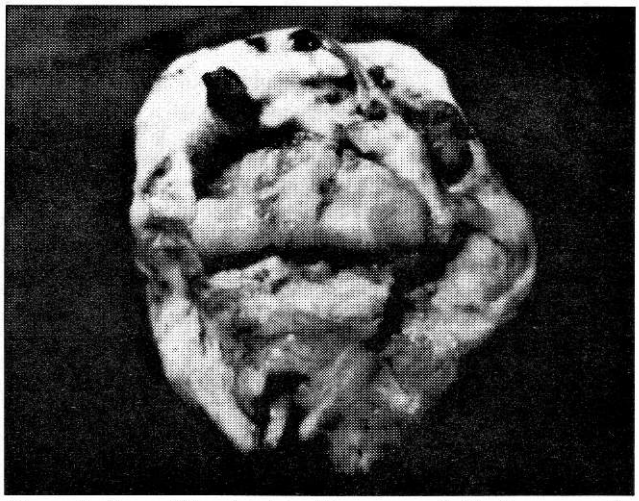

Figure 8. *Carpal (knee) joint with severe arthritis from ewe with OPP.*

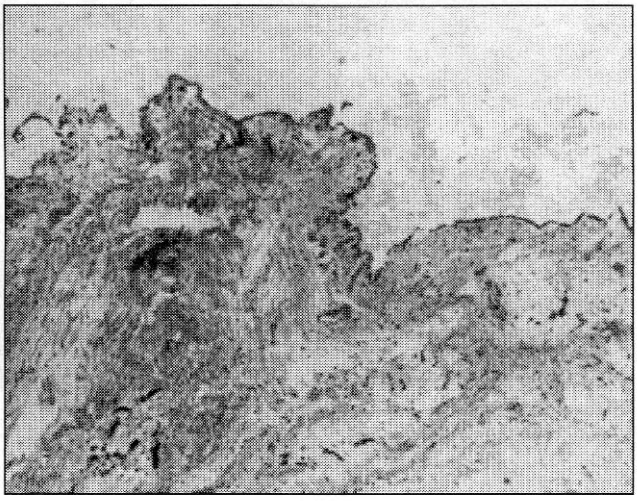

Figure 9. *Light micrograph of synovial membrane from a normal sheep.*

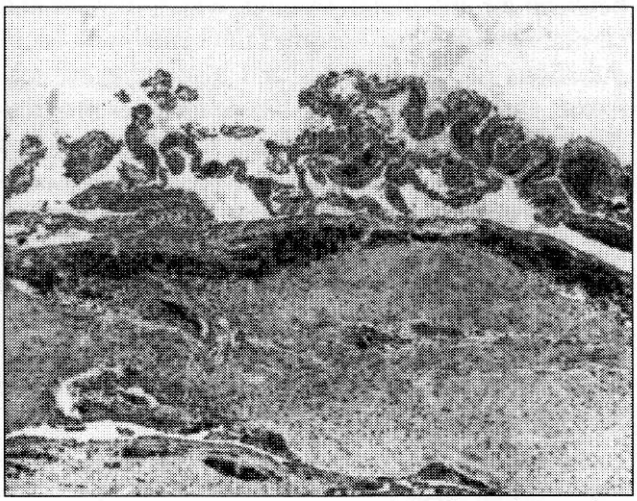

Figure 10. *Light micrograph of synovial membrane from a sheep with OPP. Note diffuse accumulation of lymphoid cells below the surface and around blood vessels of the tissue.*

examination reveals excessive numbers of lymphocytes and macrophages around blood vessels, as well as degeneration of the brain.

TRANSMISSION

Ovine progressive pneumonia virus is carried in macrophages in the tissues and fluids of sheep. Secretions from the udder and lungs that carry these cells are believed to be the main sources of virus for transmission. Other secretions such as saliva and placental fluids may be infectious, but this is not proven. Transmission through drinking water contaminated with feces from infected sheep was reported but has not been substantiated, and urine is not known to be infectious. Transmission through blood, sperm, ova, embryos, or semen has not been adequately studied and cannot be completely ruled out. Likewise, little is known about the stage of infection when a sheep is likely to spread the virus or indeed if all infected sheep spread virus. The virus cannot survive for more than a few days in the environment outside the host animal, especially in hot, dry conditions.

Several studies have shown that transmission occurs between the ewe and her lambs through the colostrum and milk. Ewes in advanced stages of the disease infect their lambs more readily than ewes in early stages of the disease. Also, the longer lambs stay with infected ewes, the greater the risk of transmission of the virus. In a flock that contained OPP virus-infected and noninfected ewes, 37 percent of the lambs born to infected ewes and 20 percent of the lambs born to noninfected ewes became infected with OPP within one year after birth. Transmission of the virus to lambs while they are in the uterus of the ewe is possible but occurs at a very low rate.

Transmission among adult animals, probably through respiratory secretions, can occur as the result of direct contact, primarily in confinement-type facilities. Such transmission was documented in a study showing that the introduction of two infected ewes into a flock of 22 seronegative ewes resulted in an 80 percent infection rate within five years. Other studies show a much lower rate of spread among mature sheep, especially among grazing sheep where transmission is rare.

DIAGNOSIS

Diagnostic criteria vary considerably, because many infected sheep never express disease. Clinical signs can be used for a tentative diagnosis, but alone they are not reliable indicators of infection or disease because many asymptomatic sheep carry the virus. In addition, signs of many other diseases mimic those of OPP. Because all serologically positive adult sheep are virus carriers, a definitive diagnosis of infection can be made by demonstrating either the presence of virus or specific antibody produced against the virus. A definitive diagnosis also requires the observation of characteristic lesions. Like most biological tests, methods to detect either virus or specific antibodies are fallible and occasionally may not detect infected sheep (false negative test) or may identify noninfected sheep as infected (false positive test).

Detection of virus has traditionally been done by culturing. This is an expensive procedure that requires 12 weeks to complete and has a sensitivity of not more than 70 percent. This method, therefore, is unsuitable as a standard diagnostic procedure.

Currently, serological tests are the most practical methods for detecting OPP. Two serological tests are commonly used: an agar-gel immunodiffusion test (AGIDT), and an enzyme-linked immunosorbency assay (ELISA) test. Of the two tests, the AGIDT is the least sensitive and therefore more prone to false negative results, but its specificity and simplicity make it the test of choice for many surveillance and control programs. This is the test most commonly used by diagnostic laboratories in the United States. Because of the higher sensitivity and complicacy of the ELISA test, precise conditions are required to avoid loss of specificity and thus false positive results. Consequently, the ELISA test is not as widely available as the AGIDT. At the time of this writing there continue to be inconsistencies among laboratories.

New techniques based on molecular biology, such as polymerase chain reaction (PCR) and antigen capture ELISA (cELISA) are currently being evaluated as methods for identifying the minute amounts of OPP viral components in blood, milk and other tissues of sheep. If these techniques can be developed and standardized, they should provide the sensitivity and specificity to identify any sheep carrying the OPP virus.

Care must be used in correctly interpreting serologic results. Actively acquired antibodies (antibodies produced by the infected sheep itself) to the OPP virus are slow to develop but with few exceptions are maintained for the life of the animal. Thus, actively acquired antibodies show that the animal carries the virus. Passively acquired anti-

bodies are obtained by a newborn lamb through the colostrum from an infected dam and are lost by six months of age. Because passively acquired antibodies cannot be distinguished from actively acquired antibodies, serologic tests are uninterpretable during the first six months of life. With the AGIDT, some seropositive sheep will become temporarily seronegative following lambing, probably because of the large quantity of antibodies lost in the colostrum. There is evidence that a few sheep with severe disease may become seronegative before death. Serological testing is, therefore, best done after six months of age and before or several weeks after lambing.

Economic Impact

The economic impact of OPP is uncertain. This uncertainty is caused by lack of scientific investigation comparing the production of OPP-infected flocks with OPP-free flocks under similar management conditions; variation in breed susceptibility and disease expression; possible existence of different OPP virus strains with different diseaseproducing potential; and the influence of related diseases.

Losses attributed to OPP occur as direct and indirect costs. Direct costs include death, premature culling, increased replacements, increase in number of orphan and slow-growing lambs because of poor milk production, decreased longevity of productive sheep, and possible decrease in fertility and in strength of wool fibers of thin ewes. Indirect effects include loss from secondary infections, loss of marketing opportunities to OPP-free flock buyers, and loss of export sales. The amount of financial loss attributed to each of these effects must be measured by individual producers.

Worldwide, the economic impact of OPP varies. In Iceland, maedi-visna is reported to have caused the death of approximately 105,000 sheep and the slaughter of another 650,000 in an attempt to eradicate the disease. The total loss was nearly 30 percent of Iceland's sheep population. In the Netherlands, maedivisna was introduced into a flock of Texel sheep and studied over a five-year period. In contrast to the situation in Icelandic sheep, clinical signs of disease and high death losses were rare in the Texel sheep, although upon inspection 70 percent of the sheep had maedivisna lesions in the udder and/or lungs.

North American studies of the effects of OPP on sheep productivity are somewhat conflicting. A study of range sheep consisting of several breeds, including Rambouillet, Targhee, Columbia and Polypay, showed that lamb and wool production of seropositive range ewes did not differ from seronegative ewes. In comparison, studies in intensively managed farm flocks found that Finnsheep and Cheviot flocks were nonproductive beyond four years of age because of disease and death ascribable to OPP. These farm flock studies also reported lower weaning weights and reduced numbers of lambs born to OPP-infected ewes. Lower conception rates and lamb birth weights attributed to OPP infection were reported in a Canadian farm flock study. Based on these reports, the degree of economic loss caused by OPP is likely associated with the type of management system, breed of sheep, and intensity of production, and is thus quite variable.

In summary, the economic impact of OPP cannot be fully understood until additional information is obtained. Before control/eradication measures are undertaken, the financial impact of OPP must be assessed at the flock level by the producer and his or her veterinarian.

Treatment and Control

No effective treatment to eliminate OPP infection is available, therefore, any treatment will be symptomatic. Producers should consult with their veterinarians for specific recommendations. Most sheep with OPP die of secondary bacterial pneumonia. Antibiotics can be used to treat or prevent secondary infections and may prolong the useful life of a sheep for a few weeks or months. Vaccines for OPP have not been successful. However, the recent success of a vaccine for Simian Immunodeficiency Virus, a lentivirus of monkeys, will encourage continued research efforts.

Some producers have successfully eradicated OPP from their flocks by either testing and removing seropositive sheep or by collecting lambs at birth and artificially rearing them in isolation.

Steps recommended in these two procedures are as follows.

■ *Method I. Test and Remove*

1. Bleed all sheep and goats on the farm and test for antibodies to OPP virus. Goats must be included because of the possible cross infection of sheep with CAE virus resulting in a positive reading of the serological test.

2. Remove all seropositive sheep and their lambs of less than one year of age from the flock. Sheep removed from the flock can either be sold or isolated in separate facilities. The procedure may also be successful when lambs of positive ewes are kept in the flock, but more time is required to eradicate the virus.
3. Keep the clean flock isolated from infected sheep and goats and, if possible, from people and equipment in contact with an infected flock.
4. Add only seronegative sheep to the flock. The additions can be either from other seronegative flocks or from seronegative parents in an infected flock following at least one year of isolation with a negative test reading.
5. Test annually until there are at least two consecutive negative flock tests to be reasonably sure that the flock is free of the virus. This must be done even when starting with a negative flock. Periodic testing is necessary to ensure that the virus has not been reintroduced into the flock. One should anticipate three to five years to eradicate OPP from an infected flock.

■ *Method II. Isolate and Artificially Rear Progeny*

1. Remove lambs from ewes before nursing and maintain them in isolation from infected sheep. Extreme care must be taken to ensure that newborns do not nurse. The ewe's teats can be "taped" to prevent nursing. The ewes must not be allowed to lick or nuzzle the lambs.
2. Proceed with steps 3 through 5 above to ensure virus-free status of the new flock. The virus can be eradicated in one year by this procedure but it is labor-intensive and expensive. An advantage is that valuable genetic stock can be preserved.

Variations of the above methods are helpful in reducing the prevalence of OPP but eradication requires careful adherence to the recommended methods. Eradication protocols for maedi-visna (OPP) in Europe advocate testing twice a year. This should hasten eradication but will also add to the expense. In any case, individual, permanent identification and meticulous recordkeeping are essential for success. An alternative to these eradication methods is to depopulate an existing flock and repopulate with sheep that have had at least two negative tests over the previous two years. If this method is chosen, producers should clean confinement and concentration areas thoroughly and wait at least one month before repopulating with clean sheep. Eradication is expensive and may not be practical in some commercial sheep operations in which a high percentage of the flock is infected but little loss is observed. For breeders of sheep for sale to "OPP-free" flock owners or for export where seronegative status is often required, the expense of an eradication program should be justifiable.

Conclusion

Ovine progressive pneumonia can occur in any breed of sheep under any management system and environmental condition. However, rates of infection and disease expression vary, as does economic impact. General control and eradication methods have proven effective. In accordance with sound livestock husbandry practices, all diseases, including OPP, should be controlled to improve the health and well-being of animals and to avoid the spread of disease to other sheep. Any decision to eradicate OPP should be made on the basis of a producer's unique conditions after careful analysis of the flock's historical production and health records in consultation with a veterinarian.

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